Effects of systolic blood pressure on white-matter integrity in young adults in the Framingham Heart Study: a cross-sectional study

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Summary

Background—Previous studies have identified effects of age and vascular risk factors on brain injury in elderly individuals. We aimed to establish whether the effects of high blood pressure in the brain are evident as early as the fifth decade of life.

Methods—In an investigation of the third generation of the Framingham Heart Study, we approached all participants in 2009 to ask whether they would be willing to undergo MRI. Consenting patients underwent clinical assessment and cerebral MRI that included T1-weighted and diffusion tensor imaging to obtain estimates of fractional anisotropy, mean diffusivity, and grey-matter volumes. All images were coregistered to a common minimum deformation template for voxel-based linear regressions relating fractional anisotropy, mean diffusivity, and grey-matter volumes to age and systolic blood pressure, with adjustment for potential confounders.

Findings—579 (14·1%) of 4095 participants in the third-generation cohort (mean age 39·2 years, SD 8·4) underwent brain MRI between June, 2009 and June, 2010. Age was associated with decreased fractional anisotropy and increased mean diffusivity in almost all cerebral white-matter voxels. Age was also independently associated with reduced grey-matter volumes. Increased systolic blood pressure was linearly associated with decreased regional fractional anisotropy and increased mean diffusivity, especially in the anterior corpus callosum, the inferior fronto-occipital fasciculi, and the fibres that project from the thalamus to the superior frontal gyrus. It was also strongly associated with reduced grey-matter volumes, particularly in Brodmann's area 48 on the medial surface of the temporal lobe and Brodmann's area 21 of the middle temporal gyrus.

Interpretation—Our results suggest that subtle vascular brain injury develops insidiously during life, with discernible effects even in young adults. These findings emphasise the need for early and optimum control of blood pressure.

Introduction

Increased blood pressure is estimated to affect 50 million people in the USA.[1] Additionally, it is associated with a 62% population attributable risk for cerebrovascular disease and a 49% attributable risk for cardiovascular disease in individuals older than 50 years, and is the greatest risk factor for mortality.[1] Despite increasing awareness, less than 60% of identified individuals receive treatment for their hypertension and adequate control of blood pressure is achieved in less than a third of those treated.[1] Systolic blood pressure (SBP) increases with age,[2] resulting in a lifetime risk for hypertension of almost 90%, which further attests to the high frequency of this disorder.[3]

Previous studies of individuals aged 60 years or older suggest that, even in people with well controlled hypertension,[4] increased SBP is associated with clinically silent brain injuries such as increased brain atrophy,[5,6] grey-matter atrophy,[7] white-matter injury[8,9] including white-matter hyperintensities (WMH),[10] and clinically asymptomatic infarcts.[11,12] These differences in brain structure are also associated with cross-sectional[5,6,9,13] and longitudinal[14,15] reductions in cognitive ability, which could begin as early as age 50 years[16] and are associated with an increased likelihood of incident dementia.[17]

With sensitive measures of white-matter injury from diffusion tensor imaging, studies from the past 5 years also suggest that increased blood pressure is associated with subtle injury to white matter, even in the absence of WMH. For example, altered fractional anisotropy can occur,[18] particularly in the anterior corpus callosum,[18–20] a region where altered fractional anisotropy is associated with cognitive impairment and dementia.[18,21,22]

Apart from clinically evident vascular events, midlife hypertension is an important modifiable risk factor for cognitive decline, mild cognitive impairment, and vascular dementia late in life.[23] Unfortunately, treatment of increased blood pressure late in life to prevent cognitive impairment has had mixed results.[24] Although the usefulness of this approach is not well established, reasonable evidence exists to suggest that in people younger than 50 years, lowering blood pressure can help to prevent cognitive decline and dementia late in life.[23]

Therefore, establishing whether midlife blood pressure differences are associated with concomitant subtle brain injury could identify the earliest changes in brain health linked to hypertension. These findings would further emphasise the importance of aggressive, early management of hypertension as a preventive strategy against cognitive decline late in life, in addition to the recognised benefits of treatment on cardiovascular and cerebrovascular events.[1]

Our aim was to explore cross-sectional associations between increased SBP,[25] age, measures of white-matter injury (fractional anisotropy and mean diffusivity), and grey-matter atrophy in the third generation of Framingham Heart Study participants. Because of the young age of the cohort, we postulated that increased SBP would be associated with lower fractional anisotropy and higher mean diffusivity values, because these measures are sensitive to white-matter pathology. We also tested whether WMH volumes and cerebral

atrophy increased, which would suggest that SBP can lead to vascular brain injury as early as the fifth decade of life.

Methods

Study design and participants

The Framingham Heart Study is a single-site, community-based, prospective cohort study in Framing ham (MA, USA) that was initiated in 1948 to investigate risk factors for cardiovascular disease. It comprises three generations of participants. Study of the 4095 participants in the third-generation cohort (G3) began in 2000, with the recruitment and first assessment occurring between 2002 and 2005. From June 2009, all individuals recruited to the G3 cohort were approached to participate in our MRI study. We excluded participants with prevalent stroke at the MRI assessment or other neurological disorders that might confound the assessment of brain volumes, or because of poor MRI quality (appendix).

The institutional review boards at all participating institutions approved the study. Patients or their legal representatives gave written informed consent.

Procedures

Participants had one MRI at baseline, when they were also monitored with previously described surveillance techniques[26,27] for the development of stroke or dementia. Stroke was defined as an acute-onset focal neurological deficit of presumed vascular aetiology lasting 24 h or more. Dementia was diagnosed according to criteria of the Diagnostic and Statistical Manual of Mental Disorders IV.[28] We recorded mean SBP and diastolic blood pressure (DBP) at time of MRI, which were calculated with two sets of values measured separately by two physicians when the patient was seated. Present smoking status was recorded in interviews. We recorded any drugs taken by each patient with prescription lists. We used three categorical variables: hypertension categories (normal: SBP <120 mm Hg and DBP <80 mm Hg; prehypertension: SBP 120–139 mm Hg or DBP 80–89 mm Hg; and hypertension: SBP 140 mm Hg or DBP 100 mm Hg) as described in the seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure;[1] whether the individual was being treated for hypertension; and smoking status at time of clinical assessment. We did not include the presence of diabetes mellitus in the models because of its low prevalence in our sample (n=7).

In addition to analysis of WMH on MRI—the burden of which is usually low in young adults—we analysed diffusion tensor imaging measures of fractional anisotropy and mean diffusivity, which are more sensitive measures of white-matter integrity than is WMH. Briefly, fractional anisotropy and mean diffusivity characterise the microstructural properties and integrity of white matter. Fractional anisotropy quantifies the amount of anisotropy of water diffusion and mean diffusivity quantifies mean water diffusion within white matter.[22]

We segmented WMH with fluid attenuated inversion recovery and grey matter with T1-weighted images by semiautomated procedures, as previously described.[29,30] All images, including fractional anisotropy, mean diffusivity, grey-matter volume, and WMH maps, were coregistered to a minimum deformation template[22,31] for group statistical analyses. Each pixel (also known as a voxel) in these coregistered volumetric images corresponds to the same location in the brain across all individuals. This correspondence allows corresponding imaging measures (fractional anisotropy or mean diffusivity measures, grey-matter density, or WMH occurrence) to be related to various independent variables. We quantified total cranial volume on the basis of fluid attenuated inversion recovery with a

previously reported analysis protocol[29] and corrected for differences in head size. WMH volumes were log transformed to normalise population variance.

Statistical analyses

The primary goal of the statistical analysis was to establish if, at the voxel level, increased SBP and age were associated with increased brain injury as indicated by decreased fractional anisotropy, raised mean diffusivity, or grey-matter atrophy. To achieve this goal, we used a linear regression with measures of fractional anisotropy, mean diffusivity, or grey-matter volumes as the dependent variable and continuous SBP and age as independent variables, adjusting for smoking status, hypertension treatment, total cranial volume, and sex. The T maps obtained for both independent variables (SBP and age) were assessed for significance with threshold-free cluster enhancement with an α of 0·05; we corrected for multiple comparisons with permutation-based correction (n=1000).[32]

We then overlaid the thresholded T maps with the Johns Hopkins University probabilistic fibre map atlases[33] and a template of Brodmann's areas, which were warped to the minimum deformation template space, to provide a post-hoc description of significant voxels in terms of the white-matter tracts or grey-matter regions to which they most probably belonged.

A second objective of our study was to estimate a global measure of brain health in individuals with prehypertension and hypertension as compared with normotensive individuals. To achieve this goal, we used the mean fractional anisotropy and mean diffusivity and the volume of grey matter in regions that had been identified in the voxel-based analysis as significantly associated with increasing SBP. We then used a principal component analysis to decompose the data into a linear combination of orthogonal, with a singular value de composition implementation.[34] The objective of this decomposition was to generate a composite measure of brain health.

The resulting first principal component (PC1) explained the greatest amount of variance in the dataset and was then used as the dependent variable in a linear regression with hypertension category and age as independent variables, adjusting for smoking status, hypertension treatment, total cranial volume, and sex. Because the PC1 measure seemed to be quadratically related to age on visual inspection, we also created a model that included a quadratic effect of age. We assessed increase in quality of quadratic fit compared with the linear fit of age with a likelihood ratio test. The interactions of SBP with age and the quadratic effect of age were tested but were not significant; therefore, we removed them from the model. Because hypertension is associated with accelerated brain ageing,[4,6] we then compared group differences in this summary measure to establish estimates of the number of years of age necessary to achieve the same mean value for the two hypertensive groups.

Finally, we explored whether WMH in young adults could provide further information about white-matter injury associated with hypertension in these participants. We did a linear regression with WMH volume as the dependent variable and SBP as the independent variable, adjusting for age, smoking status, hypertension treatment, total cranial volume, and sex.

Role of the funding source

Results

Our study includes 579 (14·1%) of 4095 participants in G3[35] who underwent brain MRI between June, 2009, and June, 2010. Compared with the rest of G3, individuals included in our study were significantly younger, had significantly lower SBP and DBP, and were less likely to be receiving treatment for hypertension (table 1). Additionally, fewer were male and they were less likely to smoke or have diabetes than were the individuals in the rest of G3 (table 1). Participants were aged 19–63 years (median 39, IQR 33–45). As expected in this sample of young adults, mean WMH volume was low (table 1).

Age was independently associated with decreased fractional anisotropy within voxels that covered 49·4 cm^3 of the white matter and SBP was associated in voxels covering 2·9 cm^3. Additionally, age was associated with increased mean diffusivity within voxels that covered 87·6 cm^3 and SBP in voxels covering 10·5 cm^3 of the white matter. High SBP was strongly associated with decreased fractional anisotropy and increased mean diffusivity within white-matter tracts such as the anterior corpus callosum, the inferior fronto-occipital fasciculi, and the fibres that project from the thalamus to the superior frontal gyrus (figures 1, 2; tables 2, 3). Age was associated with decreased fractional anisotropy and increased mean diffusivity in almost all cerebral white-matter voxels (figure 1). The anterior corpus callosum, the inferior fronto-occipital fasciculi, the inferior longitudinal fasciculus, the cingulum bundle, and the fibres that project from the thalamus to the superior frontal gyrus (table 3) had a large number of voxels that showed significant associations between age and decreased fractional anisotropy or increased mean diffusivity (figure 2; tables 2, 3).

Age was independently associated with decreased grey-matter volumes within voxels that covered 171·9 cm^3, as was SBP in voxels covering 2·9 cm^3 of grey matter (appendix). Increased SBP was strongly associated with reduced grey-matter volumes, particularly in Brodmann's area 48 on the medial surface of the temporal lobe and Brodmann's area 21 of the middle temporal gyrus (figures 2, 3). Age was diffusely associated (ie, in almost all grey-matter voxels) with reduced grey-matter volumes (appendix).

The PC1 of the principal components analysis accounted for 57% of variance. Small values of the PC1 coefficient indicate low mean fractional anisotropy and grey-matter volume, and high mean mean diffusivity (ie, greater severity of brain injury). The contributions of fractional anisotropy (principal component loading 0·62), grey matter (−0·51), and mean diffusivity (0·60) to PC1 were roughly equal.

Linear regression suggested that reduced brain integrity as expressed by PC1 was significantly associated with hypertension category and increasing age (figure 4). With the addition of a quadratic effect of age, the goodness of fit of the model rose, as indicated by the likelihood ratio test (p=0·0047). The linear (R^2=0·43) and quadratic (R^2=0·44) models explained substantial variation in the principal component. Brain integrity was usually higher in normotensive individuals (β=1·88, 95% CI 0·46–3·3) than in prehypertensive (β=1·56, 95% CI 1·37–1·75; p=0·00089) and hypertensive participants (β=1·12, 95% CI 0·74–1·51; p=0·00011). It linearly (β=−0·096, 95% CI −0·09 to 0·07; p<0·0001) and quadratically decreased (β=−0·0014, 95% CI −0·0023 to −0·00042; p=0·0047) with increasing age. Brain integrity differed between hypertension categories as a function of age (figure 4).

Linear regression indicated that WMH volume was not associated with SBP (β=−0·008, 95% CI −0·09 to 0·07; p=0·84). Figure 5 shows the spatial distribution of WMH in the sample. Although the proportion of treated hypertensive individuals in our sample was low (7%), we repeated all analyses after removal of this subgroup. The results did not differ significantly from those of previous analyses (data not shown).

Discussion

Results from our study indicate that SBP is associated with injury to white-matter microstructure and regional grey matter in healthy young adults. Injury worsened continuously as SBP increased and was significantly different between normotensive and prehypertensive individuals in some regions. Moreover, the anatomical locations of these differences at fairly young ages are similar to the distribution of WMH associated with SBP late in life[36] and are associated with decreased cognitive performance, albeit in the normal range.[13]

Previous work from the Framingham Heart Study[8,10,13,37] and other studies of elderly individuals have identified cross-sectional and longitudinal associations between midlife vascular risk factors, brain atrophy, WMH, and cognitive ability late in life (panel). Our study extends these findings by showing that raised SBP has a subtle negative effect on white-matter integrity and grey-matter volume at even young adult ages, with preferential susceptibility to specific anterior white-matter tracts and grey-matter regions even before evidence of increased WMH volumes.

Evidence of even subtle brain injury at young ages should affect how physicians think about hypertension diagnoses and treatment for two important reasons. First, our evidence strongly suggests that the effect of SBP on the brain is continuous with increasing pressure, suggesting that what might be the optimum SBP will have to be reconsidered.[38] Second, these data strongly suggest that substantial brain injury could precede clinically manifest disease, indicating that prevention of stroke or cognitive impairment due to hypertensive vascular disease might require treatment at younger ages than presently thought.[37] Although present medical treatment recommendations have had a clear effect on mean blood pressure in the population[41] and mortality from hypertension-associated vascular disease,[1] the incidence and prevalence of common hypertension-associated disorders such as myocardial infarction[42] have not been greatly changed, indicating further need for early diagnosis and individual treatment.

Although our data clearly show that brain injury occurs at fairly young ages, the cause is unclear. The biological mechanisms triggered by increased SBP are complex[43] and cannot be addressed with these data. With ageing, artery stiffening causes SBP to increase, which con tributes to loading of stiff components of the atrial wall and subsequently increases arterial stiffness.[43] This process also affects small arteries and wave reflection. One hypothesis posits that vascular dysauto-regulation due to arterial remodelling causes transient reductions in blood flow to white-matter watershed areas of vascular supply,[44] resulting in transient hyporaemia, hypoxaemia, and subtle myelin injury.[45] This hypothetical process, however, explains neither the specific vulnerability of anterior white-matter tracts to increases in SBP nor the diffuse grey-matter atrophy reported in our study and others.[4–6,18]

Understanding of the regional specificity of this association is especially important in light of a growing body of scientific literature suggesting that reduced fractional anisotropy in these regions is associated with decreased cognitive performance in individuals aged 60 years or older[46,47] and similar negative associations between cognition and brain atrophy in people with raised SBP.[5,6] Because arterial stiffness has been associated with cognitive impairment in elderly individuals,[48] studies investigating the effect of pulse wave velocity—the gold standard measure for clinical assessment of arterial stiffness in the cerebral microcirculation—are needed, as are interventional studies with cognitive deterioration as a predefined outcome to elucidate the chronology and factors linking arterial ageing, microvascular damage, and cognitive decline.

However, we recorded no effect of SBP on WMH. As previously suggested in elderly individuals, WMH could be the final stage of broadly distributed and progressive white-matter degeneration,[49] which is a process that might not be sufficiently advanced in younger individuals and would therefore be a less sensitive measure than is diffusion tensor imaging of cerebrovascular disease in this otherwise healthy young cohort.[50] This view is supported by the absence of a cross-sectional association between concurrent SBP and WMH in young individuals. Midlife SBP is strongly associated with WMH burden late in life when vascular brain injury processes have progressed to an advanced stage.[5,51,52] Further substantiation of this hypothesis will necessitate longitudinal study of how diffusion tensor imaging measures and WMH coevolve spatially and temporally from midlife onward.

Notably, we focused on measures of only SBP as a marker of vascular health for two reasons. First, in this fairly young cohort, DBP and SBP measures were highly correlated. Second, increased SBP is the most common form of hypertension and is a more robust risk factor for cardiovascular disease than is DBP, particularly after 50 years of age.[25] Additionally, we did not specifically investigate the effects of low blood pressure on brain integrity. Although evidence suggests that reduced SBP is associated with cerebral atrophy in elderly individuals,[53] this finding has not been investigated in young adults and is worthy of further research. However, our results showed an inverse monotonic relation between SBP and brain atrophy.

Our study has some limitations. First, the Framingham Heart Study cohort is mostly of white descent and therefore does not fully represent the general population of the USA.[35] Second, voluntary participation in MRI studies is often biased, with the healthiest individuals being more likely to participate, particularly in samples of older adults.[54] This second concern is probably mitigated by the fairly good health and young age of our study cohort. Third, our study is cross-sectional. Further longitudinal studies are needed to investigate whether duration of increased SBP has cumulative effects on white-matter integrity in young adults.

Despite these limitations, the public health implications of our results are clear. Our findings support the need for early and optimum control of blood pressure, which is presently neither routinely achieved[39] nor subject to testing in many randomised controlled clinical trials.[40] Whether structural brain differences associated with chronic hypertension are preventable or if they can be reversed—as in a study reporting encouraging benefits of memory training on microstructure of white matter[55]—is unclear. In view of evidence that both the degree and duration of hypertension are associated with continuous adverse effects on late-life brain injury and cognition,[5,6] early and aggressive treatment could be necessary for success.

Acknowledgments

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Panel: **Research in context**

Systematic review

We searched PubMed on Jan 15, 2012, for reports published in English of the effects of blood pressure on white-matter integrity in healthy adults and older individuals with the terms "blood pressure" and "DTI". Previous work from the Framingham Heart Study has identified cross-sectional and longitudinal associations between midlife vascular risk factors and late-life cognitive ability, strokes, brain atrophy, and white-matter hyperintensities that represent severe white-matter injury.[8,14,37] With sensitive measures of white-matter injury from diffusion tensor imaging, studies from the past 4 years[18–20] have suggested that increased blood pressure is associated with subtle injury to white matter in the anterior corpus callosum in elderly individuals, and greater injury in this region has been linked to cognitive impairment and dementia.[21,22]

Interpretation

We have shown that systolic blood pressure is associated with injury to white-matter microstructure and regional grey matter in healthy young adults. Our findings extend those of earlier studies[37,38] by indicating that white-matter injury begins before the age of 50 years. Our results emphasise the need for early and optimum control of blood pressure, which is neither routinely achieved[39] nor subject to testing in many randomised controlled clinical trials.[40]
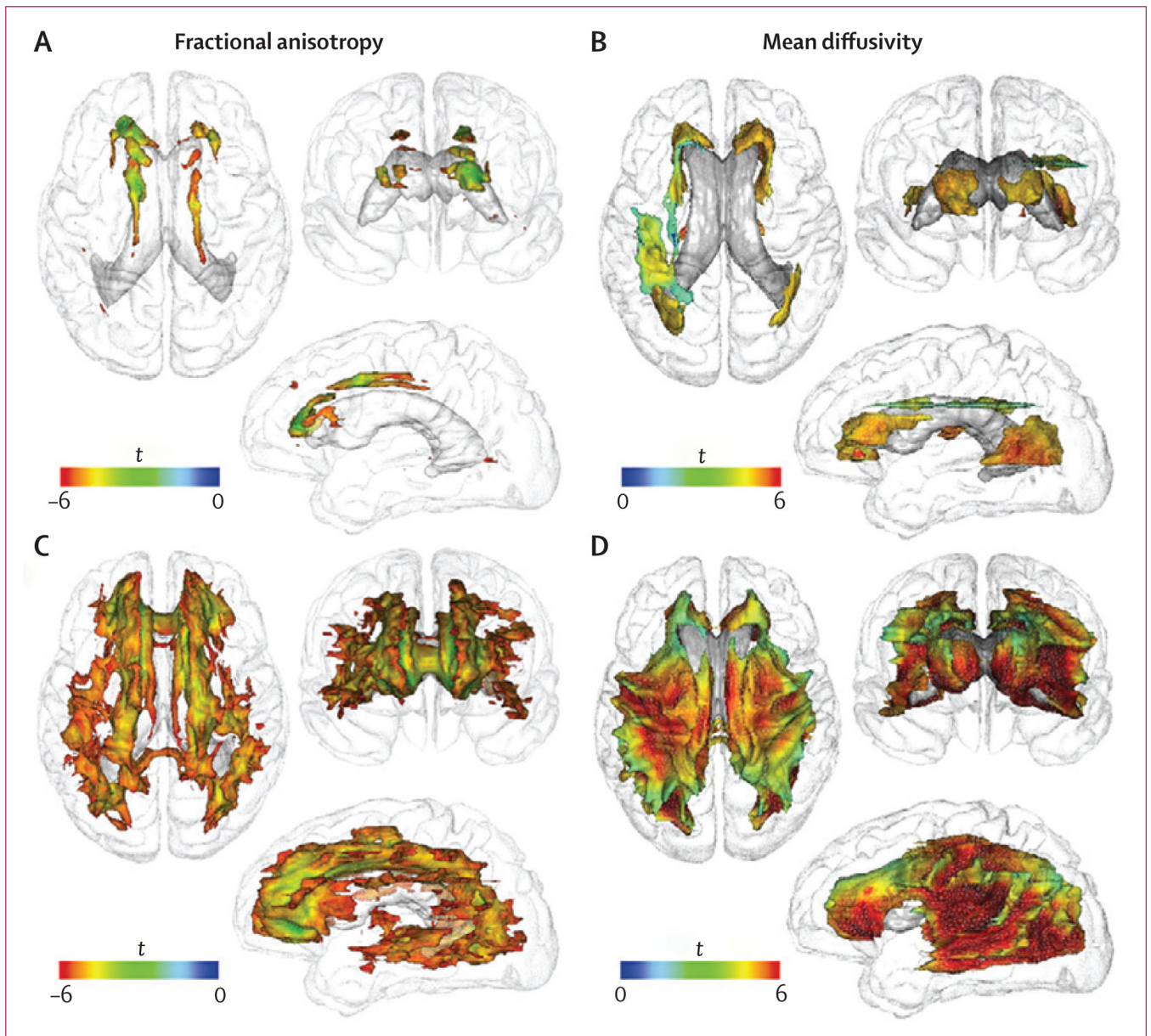
Figure 1. Regions of the cerebral white matter in which systolic blood pressure (A, B) and age (C, D) are associated with decreased fractional anisotropy and increased mean diffusivity
The voxel-based regression included diffusion tensor imaging measures (fractional anisotropy or mean diffusivity) as the dependent variable, and age and systolic blood pressure as independent variables. Number of cigarettes smoked per day, hypertension treatment (presence or absence), intracranial volume, and sex were covariates.
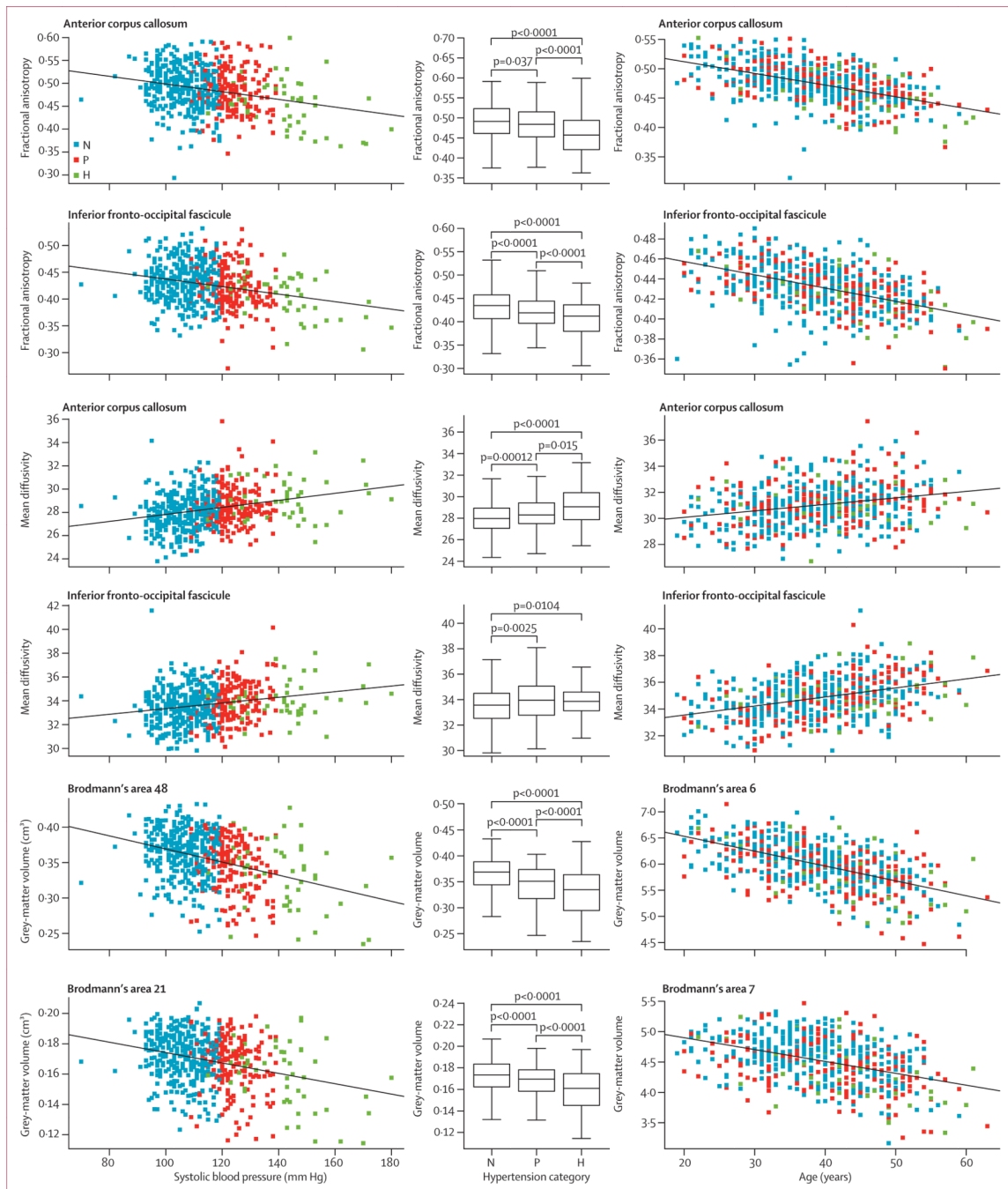
Figure 2. Regression analyses for brain areas in which associations between variables were significant and box plots showing comparisons between hypertension categories after adjustment for age

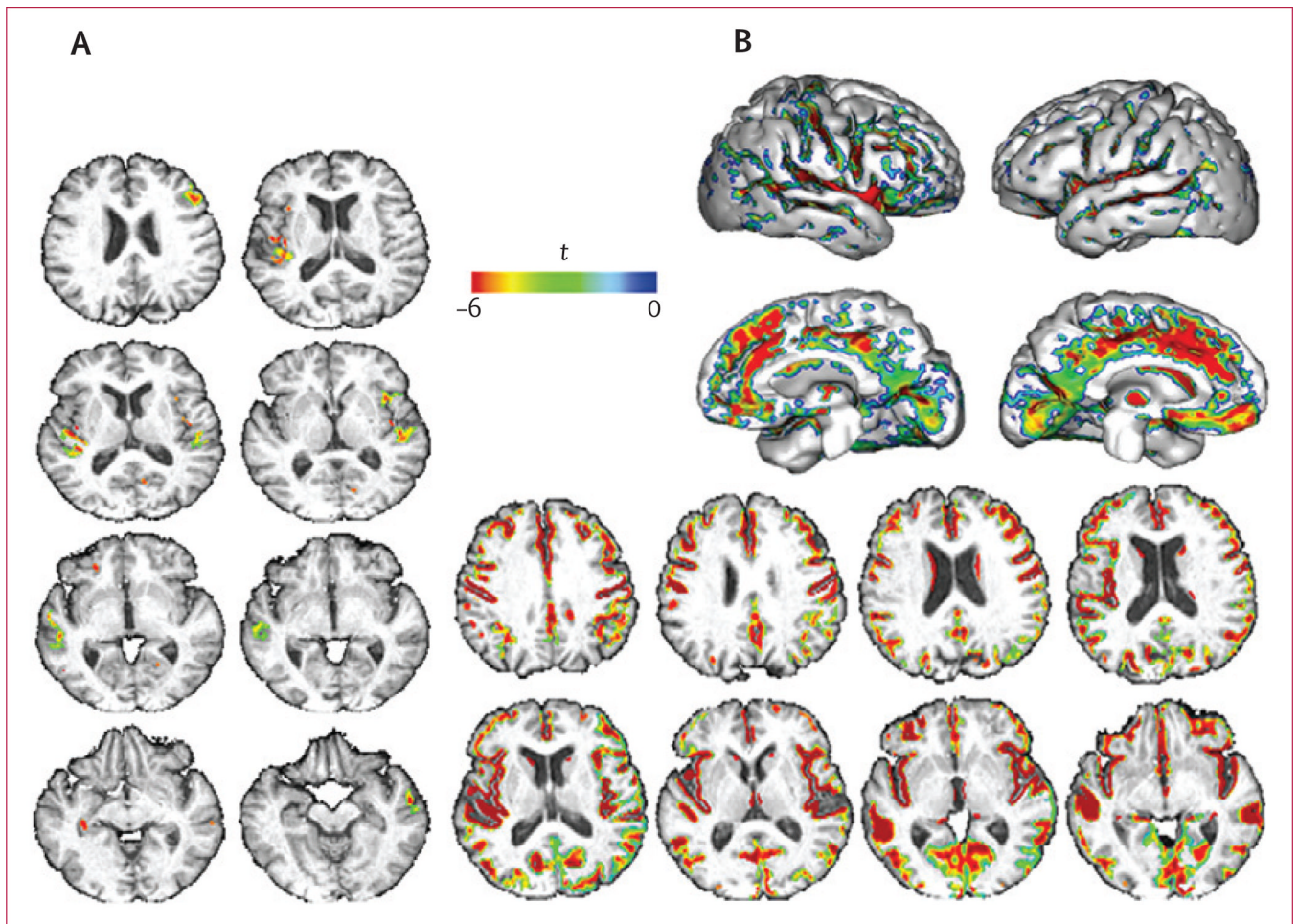N=normotensive. P=prehypertensive. H=hypertensive.

Figure 3. Cerebral regions in which decreasing grey-matter volumes were significantly associated with increasing systolic blood pressure (A) and age (B)

The voxel-based regression included grey-matter probability as the dependent variable and age and systolic blood pressure as independent variables. Number of cigarettes smoked per day, hypertension treatment (treated or not), intracranial volume, and sex were covariates.
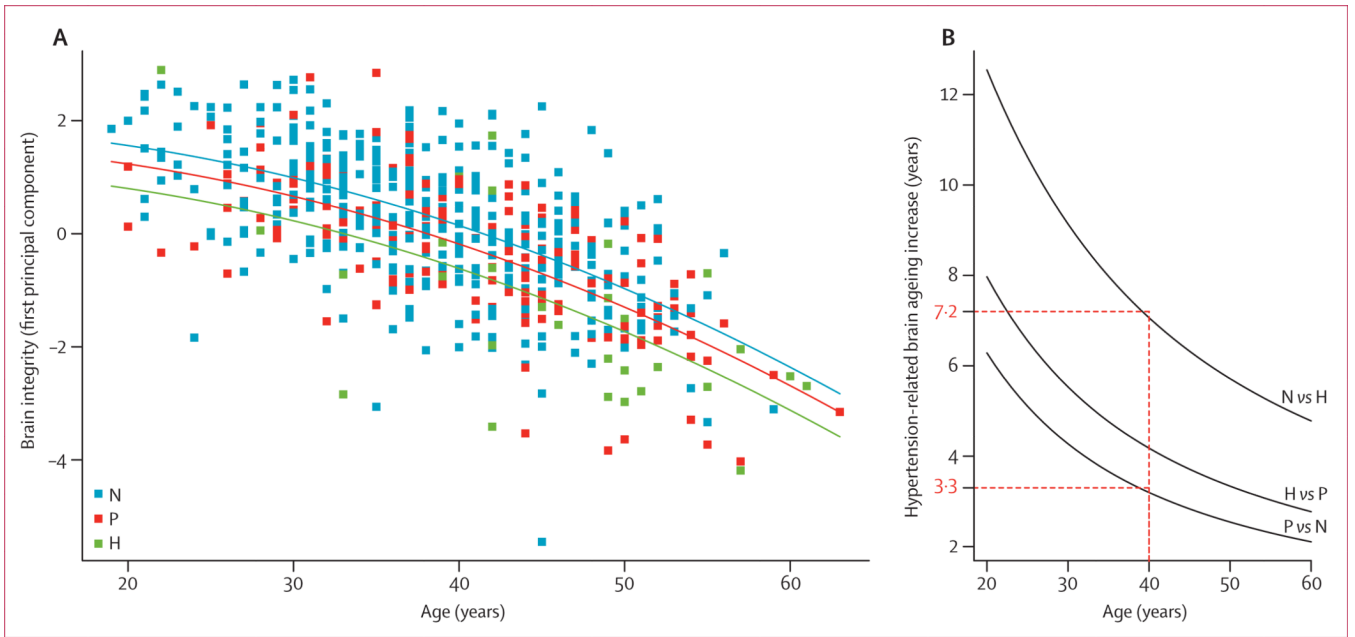
Figure 4. Regression curves relating brain integrity as expressed by the first principal component as a function of the hypertension category and age of the individual (A) and the difference in brain ageing increase between hypertension categories according to age (B)
Red dotted lines indicate brain integrity of a 40-year-old by hypertensive status; brain integrity of a 40-year-old prehypertensive individual corresponded to that of a normotensive individual 3·3 years older, but this difference was 7·2 years for hypertensive individuals. N=normotensive. P=prehypertensive. H=hypertensive.
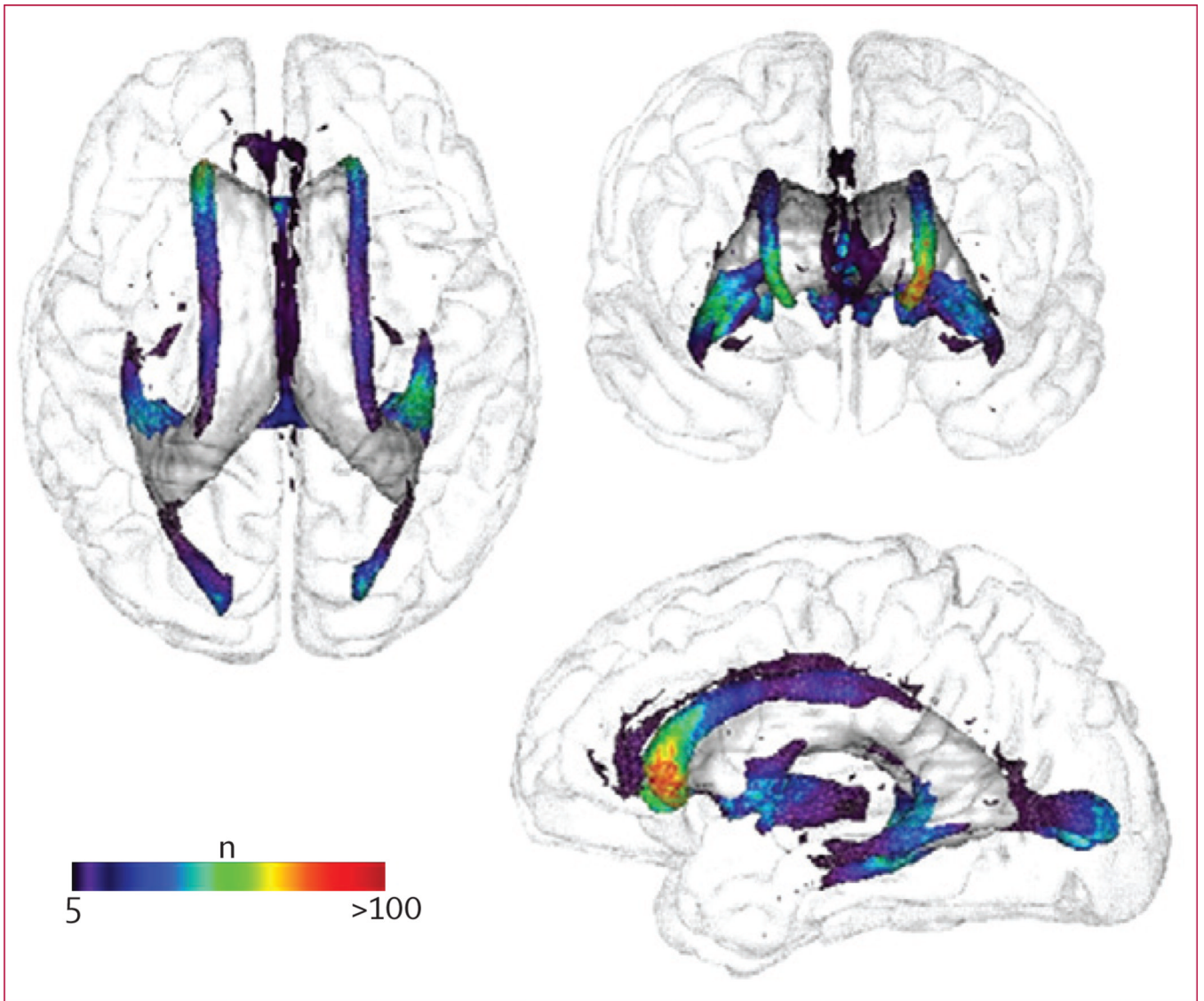
Figure 5. Number of patients with white-matter hyperintensities at a voxel location

Table 1

Characteristics of participant

	DTI sample[*] (n=579)	Rest of G3 (n=3516)	p value
Age (years)	39·2 (8·4)	40·3 (8·9)	0·005
Systolic blood pressure (mm Hg)	115 (14)	117 (14)	0·001
Diastolic blood pressure (mm Hg)	74 (10)	76 (10)	0·001
Women	345 (59·6%)	1838 (52·5%)	0·001
Current smoking	62 (10·7%)	573 (16·3%)	0·001
Hypertension treatment	41 (7·1%)	393 (11·2%)	0·003
Diabetes	7 (1·2%)	117 (3·3%)	0·006
Prevalent cardiovascular disease	4 (0·7%)	62 (1.8%)	0·003
Atrial fibrillation	2 (0·4%)	17 (0·5%)	0·65
White-matter hyperintensities (cm^3)	1·7 (1·0)	NA	NA
Total intracranial volume (cm^3)	1232·8 (147·5)	NA	NA

Data are mean (SD) or n (%), unless otherwise stated. DTI=diffusion tensor imaging. NA=not applicable.

[*] Individuals in our study who underwent an MRI examination including DTI acquisition.

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Table 2

Associations between decreasing fractional anisotropy and increasing systolic blood pressure and age by fibre label

	Total number of voxels	Number of voxels associated with increasing systolic blood pressure	Number of voxels associated with age
Corpus callosum [*]			
Medial occipital gyrus	2454	0	526
Post-central gyrus	1707	18	417
Pre-central gyrus	2159	89	747
Rectus	537	0	382
Superior frontal gyrus	15 550	1220	9117
Superior occipital gyrus	4336	0	1288
Superior parietal gyrus	4959	0	951
Cingulum	5873	150	2622
Corticospinal tract	5788	0	842
Inferior fronto-occipital tract	9121	304	4124
Inferior longitudinal fasciculus	7896	20	2417
Short association fibres			
Inferior occipital gyrus	2021	0	539
Superior frontal gyrus and supramarginal gyrus	5013	14	1070
Superior parietal gyrus and angular gyrus	4038	0	391
Superior longitudinal fasciculus			
Frontal and parietal	4815	0	706
Frontal and temporal	2682	0	442
Parietal and temporal	5341	0	1268
Thalamic radiations [†]			
Middle frontal gyrus	1638	46	460
Superior frontal gyrus	7374	142	1494
Uncinate	3444	42	1509

Data are n. Regions of interest listed here only when the number of voxels associated with systolic blood pressure or age made up at least 1% of the total number of associated voxels. Fibre labels according to the Johns Hopkins University probabilistic fibre map atlases.[33]

[*] Labels refer to fibres connecting the cortical areas in both hemispheres through the corpus callosum.

[†] Labels indicate fibres that project from the thalamus.

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Table 3

Associations between increasing mean diffusivity and increasing systolic blood pressure and age by fibre label

	Total number of voxels	Number of voxels associated with increasing systolic blood pressure	Number of voxels associated with increasing age
Corpus callosum [*]			
Medial occipital gyrus	2454	282	1758
Post-central gyrus	1707	0	909
Pre-central gyrus	2159	0	1193
Rectus	537	96	201
Superior frontal gyrus	15 550	1051	4644
Superior occipital gyrus	4336	391	3035
Superior parietal gyrus	4959	34	3081
Cingulum	5873	14	3253
Corticospinal tract	5788	62	2763
Inferior fronto-occipital tract	9121	1828	5102
Inferior longitudinal fasciculus	7896	263	4358
Short association fibres			
Inferior occipital gyrus	2021	0	710
Superior frontal gyrus and supramarginal gyrus	3904	0	1269
Postcentral gyrus	1758	4	873
Precentral gyrus	3326	0	1166
Superior parietal gyrus and angular gyrus	4038	37	1811
Superior parietal and middle occipital gyrus	857	19	666
Superior longitudinal fasciculus			
Frontal and parietal	4815	181	3143
Frontal and temporal	2682	441	2101
Parietal and temporal	5341	383	3253
Thalamic radiations [†]			
Inferior frontal	401	121	175
Middle frontal gyrus	1638	404	1024
Post-central gyrus	1408	34	1113
Pre-central gyrus	1992	120	1650
Superior frontal gyrus	7374	978	5201
Superior occipital gyrus	989	76	518
Superior parietal gyrus	1722	77	1401
Uncinate	3444	425	620

Data are n. Regions of interest listed here only when the number of voxels associated with systolic blood pressure or age made up at least 1% of the total number of associated voxels. Fibre labels according to the Johns Hopkins University probabilistic fibre map atlases.[33]

*
Labels refer to fibres connecting the cortical areas in both hemispheres through the corpus callosum.

†
Labels indicate fibres that project from the thalamus.